

CLAIMS

1. A polypeptide comprising an immunogenic portion of a soluble *M. tuberculosis* antigen, or a variant of said antigen that differs only in conservative substitutions and/or modifications, wherein said antigen has an N-terminal sequence selected from the group consisting of:

- (a) Asp-Pro-Val-Asp-Ala-Val-Ile-Asn-Thr-Thr-Cys-Asn-Tyr-Gly-Gln-Val-Val-Ala-Ala-Leu; (SEQ ID No. 120)
- (b) Ala-Val-Glu-Ser-Gly-Met-Leu-Ala-Leu-Gly-Thr-Pro-Ala-Pro-Ser; (SEQ ID No. 121)
- (c) Ala-Ala-Met-Lys-Pro-Arg-Thr-Gly-Asp-Gly-Pro-Leu-Glu-Ala-Ala-Lys-Glu-Gly-Arg; (SEQ ID No. 122)
- (d) Tyr-Tyr-Trp-Cys-Pro-Gly-Gln-Pro-Phe-Asp-Pro-Ala-Trp-Gly-Pro; (SEQ ID No. 123)
- (e) Asp-Ile-Gly-Ser-Glu-Ser-Thr-Glu-Asp-Gln-Gln-Xaa-Ala-Val; (SEQ ID No. 124)
- (f) Ala-Glu-Glu-Ser-Ile-Ser-Thr-Xaa-Glu-Xaa-Ile-Val-Pro; (SEQ ID No. 125)
- (g) Asp-Pro-Glu-Pro-Ala-Pro-Pro-Val-Pro-Thr-Thr-Ala-Ala-Ser-Pro-Pro-Ser; (SEQ ID No. 126)
- (h) Ala-Pro-Lys-Thr-Tyr-Xaa-Glu-Glu-Leu-Lys-Gly-Thr-Asp-Thr-Gly; (SEQ ID No. 127)
- (i) Asp-Pro-Ala-Ser-Ala-Pro-Asp-Val-Pro-Thr-Ala-Ala-Gln-Leu-Thr-Ser-Leu-Leu-Asn-Ser-Leu-Ala-Asp-Pro-Asn-Val-Ser-Phe-Ala-Asn; (SEQ ID No. 128) and
- (j) Ala-Pro-Glu-Ser-Gly-Ala-Gly-Leu-Gly-Gly-Thr-Val-Gln-Ala-Gly; (SEQ ID No. 136)

wherein Xaa may be any amino acid.

2. A polypeptide comprising an immunogenic portion of an *M. tuberculosis* antigen, or a variant of said antigen that differs only in conservative

substitutions and/or modifications, wherein said antigen has an N-terminal sequence selected from the group consisting of:

- (a) Asp-Pro-Pro-Asp-Pro-His-Gln-Xaa-Asp-Met-Thr-Lys-Gly-Tyr-Tyr-Pro-Gly-Gly-Arg-Arg-Xaa-Phe; (SEQ ID No. 129) and
- (b) Xaa-Tyr-Ile-Ala-Tyr-Xaa-Thr-Thr-Ala-Gly-Ile-Val-Pro-Gly-Lys-Ile-Asn-Val-His-Leu-Val; (SEQ ID No. 137), wherein Xaa may be any amino acid.

3. A polypeptide comprising an immunogenic portion of a soluble *M. tuberculosis* antigen, or a variant of said antigen that differs only in conservative substitutions and/or modifications, wherein said antigen comprises an amino acid sequence encoded by a DNA sequence selected from the group consisting of the sequences recited in SEQ ID Nos.: 1, 2, 4-10, 13-25, 52, 99 and 101, the complements of said sequences, and DNA sequences that hybridize to a sequence recited in SEQ ID Nos.: 1, 2, 4-10, 13-25, 52, 99 and 101 or a complement thereof under moderately stringent conditions.

4. A polypeptide comprising an immunogenic portion of a *M. tuberculosis* antigen, or a variant of said antigen that differs only in conservative substitutions and/or modifications, wherein said antigen comprises an amino acid sequence encoded by a DNA sequence selected from the group consisting of the sequences recited in SEQ ID Nos.: 26-51, 138, 139, 163-183, 201, 240, 242-247, 253-256, 295-298, 309, 316, 318-320, 322, 324, 328, 329, 333, 335, 337, 339 and 341, the complements of said sequences, and DNA sequences that hybridize to a sequence recited in SEQ ID Nos.: 26-51, 138, 139, 163-183, 201, 240, 242-247, 253-256, 295-298, 309, 316, 318-320, 322, 324, 328, 329, 333, 335, 337, 339 and 341 or a complement thereof under moderately stringent conditions.

5. A DNA molecule comprising a nucleotide sequence encoding a polypeptide according to any one of claims 1-4.

6. An expression vector comprising a DNA molecule according to claim 5.

7. A host cell transformed with an expression vector according to claim 6.

8. The host cell of claim 7 wherein the host cell is selected from the group consisting of *E. coli*, yeast and mammalian cells.

9. A pharmaceutical composition comprising one or more polypeptides according to any one of claims 1-4 and a physiologically acceptable carrier.

10. A pharmaceutical composition comprising one or more DNA molecules according to claim 5 and a physiologically acceptable carrier.

11. A pharmaceutical composition comprising one or more DNA sequences recited in SEQ ID Nos.: 3, 11, 12, 140, 141, 156-160, 189-193, 199, 200, 203, 215-225, 237, 239, 261-276, 292, 293, 303-308, 310-315, 317, 321, 323, 325-327, 330-332, 334, 336, 338, 340 and 342-347; and a physiologically acceptable carrier.

12. A vaccine comprising one or more polypeptides according to any one of claims 1-4 and a non-specific immune response enhancer.

13. A vaccine comprising:
a polypeptide having an N-terminal sequence selected from the group consisting of sequences recited in SEQ ID NO: 134 and 135; and
a non-specific immune response enhancer.

14. A vaccine comprising:
one or more polypeptides encoded by a DNA sequence selected from the group consisting of SEQ ID Nos.: 3, 11, 12, 140, 141, 156-160, 189-193, 199, 200, 203, 215-225, 237, 239, 261-276, 292, 293, 303-308, 310-315, 317, 321, 323, 325-327, 330-332, 334, 336, 338, 340 and 342-347, the complements of said sequences, and DNA sequences that hybridize to a sequence recited in SEQ ID Nos.: 3, 11, 12, 140, 141, 156-160, 189-193, 199, 200, 203, 215-225, 237, 239, 261-276, 292, 293, 303-308, 310-315, 317, 321, 323, 325-327, 330-332, 334, 336, 338, 340 and 342-347; and

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a non-specific immune response enhancer.

15. The vaccine of claims 12-14 wherein the non-specific immune response enhancer is an adjuvant.

16. A vaccine comprising one or more DNA molecules according to claim 5 and a non-specific immune response enhancer.

17. A vaccine comprising one or more DNA sequences recited in SEQ ID Nos.: 3, 11, 12, 140, 141, 156-160, 189-193, 199, 200, 203, 215-225, 237, 239, 261-276, 292, 293, 303-308, 310-315, 317, 321, 323, 325-327, 330-332, 334, 336, 338, 340 and 342-347; and a non-specific immune response enhancer.

18. The vaccine of claims 16 or 17 wherein the non-specific immune response enhancer is an adjuvant.

19. A method for inducing protective immunity in a patient, comprising administering to a patient a pharmaceutical composition according to any one of claims 9-11.

20. A method for inducing protective immunity in a patient, comprising administering to a patient a vaccine according to any one of claims 12-18.

21. A fusion protein comprising two or more polypeptides according to any one of claims 1-4.

22. A fusion protein comprising one or more polypeptides according to any one of claims 1-4 and ESAT-6.

23. A fusion protein comprising one or more polypeptides according to any one of claims 1-4 and the *M. tuberculosis* antigen 38 kD (SEQ ID NO:15).

24. A pharmaceutical composition comprising a fusion protein according to any one of claims 21-23 and a physiologically acceptable carrier.

25. A vaccine comprising a fusion protein according to any one of claims 21-23 and a non-specific immune response enhancer.

26. The vaccine of claim 25 wherein the non-specific immune response enhancer is an adjuvant.

27. A method for inducing protective immunity in a patient, comprising administering to a patient a pharmaceutical composition according to claim 24.

28. A method for inducing protective immunity in a patient, comprising administering to a patient a vaccine according to claims 25 or 26.

29. A method for detecting tuberculosis in a patient, comprising:

- (a) contacting dermal cells of a patient with one or more polypeptides according to any one of claims 1-4; and
- (b) detecting an immune response on the patient's skin and therefrom detecting tuberculosis in the patient.

30. A method for detecting tuberculosis in a patient, comprising:

- (a) contacting dermal cells of a patient with a polypeptide having an N-terminal sequence selected from the group consisting of sequences recited in SEQ ID NO: 134 and 135; and
- (b) detecting an immune response on the patient's skin and therefrom detecting tuberculosis in the patient.

31. A method for detecting tuberculosis in a patient, comprising:
(a) contacting dermal cells of a patient with one or more polypeptides encoded by a DNA sequence selected from the group consisting of SEQ ID Nos.: 3, 11, 12, 140, 141, 156-160, 189-193, 199, 200, 203, 215-225, 237, 239, 261-276, 292, 293, 303-308.

310-315, 317, 321, 323, 325-327, 330-332, 334, 336, 338, 340 and 342-347, the complements of said sequences, and DNA sequences that hybridize to a sequence recited in SEQ ID Nos.: 3, 11, 12, 140, 141, 156-160, 189-193, 199, 200, 203, 215-225, 237, 239, 261-276, 292, 293, 303-308, 310-315, 317, 321, 323, 325-327, 330-332, 334, 336, 338, 340 and 342-347; and

(b) detecting an immune response on the patient's skin and therefrom detecting tuberculosis in the patient.

32. The method of any one of claims 29-31 wherein the immune response is induration.

33. A diagnostic kit comprising:

- (a) a polypeptide according to any one of claims 1-4; and
- (b) apparatus sufficient to contact said polypeptide with the dermal cells of a patient.

34. A diagnostic kit comprising:

(a) a polypeptide having an N-terminal sequence selected from the group consisting of sequences recited in SEQ ID NO: 134 and 135; and

(b) apparatus sufficient to contact said polypeptide with the dermal cells of a patient.

35. A diagnostic kit comprising:

(a) a polypeptide encoded by a DNA sequence selected from the group consisting of SEQ ID Nos.: 3, 11, 12, 140, 141, 156-160, 189-193, 199, 200, 203, 215-225, 237, 239, 261-276, 292, 293, 303-308, 310-315, 317, 321, 323, 325-327, 330-332, 334, 336, 338, 340 and 342-347, the complements of said sequences, and DNA sequences that hybridize to a sequence recited in SEQ ID Nos.: 3, 11, 12, 140, 141, 156-160, 189-193, 199, 200, 203, 215-225, 237, 239, 261-276, 292, 293, 303-308, 310-315, 317, 321, 323, 325-327, 330-332, 334, 336, 338, 340 and 342-347; and

(b) apparatus sufficient to contact said polypeptide with the dermal cells of a patient.

36. A diagnostic kit comprising:

- (a) a fusion protein according to any one of claims 21-23; and
- (b) apparatus sufficient to contact said fusion protein with the dermal cells of a patient.

37. A fusion protein according to claim 23 comprising an amino acid sequence selected from the group consisting of sequences recited in SEQ ID NO: 153, 209, 351 and 355.

add A2

add C'